No additional fees are believed due, however, the Commissioner is hereby authorized to charge any additional fees that may be required or credit any overpayment to Deposit Account No. 14-0629.

I. AMENDMENTS

Please amend the application as follows:

A. In the Specification

Please delete the paragraph starting at page 5, line 18.

B. In the Claims

Please cancel claims 1-15 without prejudice.

Please add the following new claims.

50. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P4 and P5 of the ATIII, wherein P4 and P5 are the fourth and fifth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; phenylalanine; glycine; and proline, and wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; phenylalanine; glycine; and proline, wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

51. (New) The elastase-resistant ATIII of claim 50, wherein the ATIII further comprises three additional modifications, wherein the modifications occur at positions P6, P7, and P8 of the ATIII, wherein P6, P7, and P8 are the sixth, seventh, and eighth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P8 is glutamic acid, wherein residue P7 comprises an amino acid selected from the group consisting of glutamic acid and glutamine, and wherein P6 comprises an amino acid selected from the group consisting of: leucine; glycine; glutamic acid; and threonine.

B1 cont

52. (New) The elastase-resistant ATIII of claim 50, wherein the ATIII further comprises one additional modification, wherein the modification occurs at position P3 of the ATIII, wherein P3 is the third amino acid towards the amino terminal side of the scissile bond of the reactive center, and wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine.

53. (New) An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P4, P5, and P6 of the ATIII, wherein P4, P5, and P6 are the fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; phenylalanine; glycine; and proline, wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; phenylalanine; glycine; and proline, and wherein P6 comprises an amino acid selected from the group consisting of leucine, glycine, glutamic acid, and threonine, wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

54. (New) The elastase-resistant ATIII of claim 53, wherein P6 is glycine.

55. (New) The elastase-resistant ATIII of claim 54, wherein P5 is phenylalanine or glutamic acid.

56. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P3 and P6 of the ATIII, wherein P3 and P6 are the third and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine, and wherein P6 comprises an amino acid selected from the group consisting of leucine; glycine; glutamic acid; and threonine, wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

57. (New) The elastase-resistant ATIII of claim 56, wherein P3 is serine.

58. (New) The elastase-resistant ATIII of claim 56, wherein P6 is glycine.

59. (New) The elastase-resistant ATIII of claim 58, wherein P3 is serine.

60. (New) An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P3, P6, and P7 of the ATIII, wherein P3, P6, and P7 are the third, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine,

wherein P6 comprises an amino acid selected from the group consisting of leucine; glycine; glutamic acid; and threonine, and wherein P7 comprises an amino acid selected from the group consisting of glutamic acid and glutamine, wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

61. (New) The elastase-resistant ATIII of claim 60, wherein P7 is glutamic acid.

62. (New) The elastase-resistant ATIII of claim 61, wherein P3 is serine, and wherein P6 is glycine.

B/cont

63. (New) An elastase-resistant antithrombin III (ATIII) comprising at least five amino acid modifications, wherein the modifications occur at positions P3, P4, P5, P6, and P7 of the ATIII, wherein P3, P4, P5, P6, and P7 are the third, fourth, fifth, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is serine, wherein P4 is phenylalanine, wherein P5 is phenylalanine, wherein P6 is glycine, and wherein P7 is glutamic acid, wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

64. (New) An elastase-resistant antithrombin III (ATIII) comprising at least five amino acid modifications, wherein the modifications occur at positions P3, P4, P5, P6, and P7 of the ATIII, wherein P3, P4, P5, P6, and P7 are the third, fourth, fifth, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is serine, wherein P4 is alanine, wherein P5 is glutamic acid, wherein P6 is glycine, and wherein P7 is glutamic acid, wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

65. (New) An elastase-resistant antithrombin III comprising an amino acid sequence at residues 387 through 391 of SEQ ID NO:35, wherein the corresponding residues of SEQ ID NO:4 have the sequence shown at residues 3 through 7 of SEQ ID NO:4.

66. (New) An elastase-resistant antithrombin III comprising an amino acid sequence at residues 387 through 391 of SEQ ID NO:35, wherein the corresponding residues of SEQ ID NO:4 have the sequence shown at residues 3 through 7 of SEQ ID NO:5.

67. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P4 and P5 of the ATIII, wherein P4 and P5 are the fourth and fifth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; glycine; and proline, and wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; glycine; and proline, wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

68. (New) An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P4, P5, and P6 of the ATIII, wherein P4, P5, and P6 are the fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 is alanine, wherein P5 is glutamic acid; and wherein P6 is leucine, wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

69. (New) An elastase-resistant antithrombin III (ATIII) comprising at least four modifications, wherein the modifications occur at positions P3, P4, P5, and P6 of the ATIII,

wherein P3, P4, P5, and P6 are the third, fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is isoleucine, wherein P4 is alanine, wherein P5 is glutamic acid; and wherein P6 is leucine, wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1}$ x 10^3.

70. (New) The ATIII of claim 50, wherein the ATIII is in a pharmaceutically acceptable formulation.

71. (New) The elastase-resistant ATIII of claim 50, wherein the ATIII has enhanced heparin binding activity.

B1 cont.

72. (New) The ATIII of claim 71, wherein the ATIII is in a pharmaceutically acceptable formulation.

73. (New) The elastase-resistant ATIII of claim 50, wherein the ATIII has enhanced heparin binding activity, and wherein the ATIII has a mutation two residues subsequent to a glycosylation site.

74. (New) The ATIII of claim 73, wherein the ATIII is in a pharmaceutically acceptable formulation.

75. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P4 and P5 of the ATIII, wherein P4 and P5 are the fourth and fifth amino acids towards the amino terminal side of the scissile

bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; phenylalanine; glycine; and proline, and wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; phenylalanine; glycine; and proline, wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

76. (New) The elastase-resistant ATIII of claim 75, wherein the ATIII further comprises three additional modifications, wherein the modifications occur at positions P6, P7, and P8 of the ATIII, wherein P6, P7, and P8 are the sixth, seventh, and eighth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P8 is glutamic acid, wherein residue P7 comprises an amino acid selected from the group consisting of glutamic acid and glutamine, and wherein P6 comprises an amino acid selected from the group consisting of: leucine; glycine; glutamic acid; and threonine.

77. (New) The elastase-resistant ATIII of claim 75, wherein the ATIII further comprises one additional modification, wherein the modification occurs at position P3 of the ATIII, wherein P3 is the third amino acid towards the amino terminal side of the scissile bond of the reactive center, and wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine.

78. (New) An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P4, P5, and P6 of the ATIII, wherein P4, P5, and P6 are the fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino

acid selected from the group consisting of alanine; phenylalanine; glycine; and proline, wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; phenylalanine; glycine; and proline, and wherein P6 comprises an amino acid selected from the group consisting of leucine, glycine, glutamic acid, and threonine, wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

79. (New) The elastase-resistant ATIII of claim 78, wherein P6 is glycine.

80. (New) The elastase-resistant ATIII of claim 79, wherein P5 is phenylalanine or glutamic acid.

B1 cont.

81. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P3 and P6 of the ATIII, wherein P3 and P6 are the third and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine, and wherein P6 comprises an amino acid selected from the group consisting of leucine; glycine; glutamic acid; and threonine, wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

82. (New) The elastase-resistant ATIII of claim 81, wherein P3 is serine.

83. (New) The elastase-resistant ATIII of claim 81, wherein P6 is glycine.

84. (New) The elastase-resistant ATIII of claim 83, wherein P3 is serine.

85. (New) An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P3, P6, and P7 of the ATIII, wherein P3, P6, and P7 are the third, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine, wherein P6 comprises an amino acid selected from the group consisting of leucine; glycine; glutamic acid; and threonine, and wherein P7 comprises an amino acid selected from the group consisting of glutamic acid and glutamine, wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

86. (New) The elastase-resistant ATIII of claim 85, wherein P7 is glutamic acid.

87. (New) The elastase-resistant ATIII of claim 86, wherein P3 is serine, and wherein P6 is glycine.

88. (New) An elastase-resistant antithrombin III (ATIII) comprising at least five amino acid modifications, wherein the modifications occur at positions P3, P4, P5, P6, and P7 of the ATIII, wherein P3, P4, P5, P6, and P7 are the third, fourth, fifth, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is serine, wherein P4 is phenylalanine, wherein P5 is phenylalanine, wherein P6 is glycine, and wherein P7 is glutamic acid, wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

89. (New) An elastase-resistant antithrombin III (ATIII) comprising at least five amino acid modifications, wherein the modifications occur at positions P3, P4, P5, P6, and

P7 of the ATIII, wherein P3, P4, P5, P6, and P7 are the third, fourth, fifth, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is serine, wherein P4 is alanine, wherein P5 is glutamic acid, wherein P6 is glycine, and wherein P7 is glutamic acid, wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

90. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P4 and P5 of the ATIII, wherein P4 and P5 are the fourth and fifth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; glycine; and proline, and wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; glycine; and proline, wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

91. (New). An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P4, P5, and P6 of the ATIII, wherein P4, P5, and P6 are the fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 is alanine, wherein P5 is glutamic acid; and wherein P6 is leucine, wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1} \times 10^3$.

92. (New). An elastase-resistant antithrombin III (ATIII) comprising at least four modifications, wherein the modifications occur at positions P3, P4, P5, and P6 of the ATIII, wherein P3, P4, P5, and P6 are the third, fourth, fifth, and sixth amino acids towards the

amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is isoleucine, wherein P4 is alanine, wherein P5 is glutamic acid; and wherein P6 is leucine, wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1}$ x 10^3.

93. (New) The ATIII of claim 75, wherein the ATIII is in a pharmaceutically acceptable formulation.

94. (New) The elastase-resistant ATIII of any one claims 75, wherein the ATIII has enhanced heparin binding activity.

95. (New) The ATIII of claim 94, wherein the ATIII is in a pharmaceutically acceptable formulation.

96. (New) The elastase-resistant ATIII of claim 75, wherein the ATIII has enhanced heparin binding activity, and wherein the ATIII has a mutation two residues subsequent to a glycosylation site.

97. (New) The ATIII of claim 96, wherein the ATIII is in a pharmaceutically acceptable formulation.

98. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P4 and P5 of the ATIII, wherein P4 and P5 are the fourth and fifth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from

the group consisting of alanine; phenylalanine; glycine; and proline, and wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; phenylalanine; glycine; and proline, wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity.

99. (New) The elastase-resistant ATIII of claim 98, wherein the ATIII further comprises three additional modifications, wherein the modifications occur at positions P6, P7, and P8 of the ATIII, wherein P6, P7, and P8 are the sixth, seventh, and eighth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P8 is glutamic acid, wherein residue P7 comprises an amino acid selected from the group consisting of glutamic acid and glutamine, and wherein P6 comprises an amino acid selected from the group consisting of: leucine; glycine; glutamic acid; and threonine.

B1 cont.

100. (New) The elastase-resistant ATIII of claim 98, wherein the ATIII further comprises one additional modification, wherein the modification occurs at position P3 of the ATIII, wherein P3 is the third amino acid towards the amino terminal side of the scissile bond of the reactive center , and wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine.

101. (New) An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P4, P5, and P6 of the ATIII, wherein P4, P5, and P6 are the fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; phenylalanine; glycine; and proline,

wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; phenylalanine; glycine; and proline, and wherein P6 comprises an amino acid selected from the group consisting of leucine, glycine, glutamic acid, and threonine, wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity.

B1 cont.

102. (New) The elastase-resistant ATIII of claim 101, wherein P6 is glycine.

103. (New) The elastase-resistant ATIII of claim 102, wherein P5 is phenylalanine or glutamic acid.

104. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P3 and P6 of the ATIII, wherein P3 and P6 are the third and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine, and wherein P6 comprises an amino acid selected from the group consisting of leucine; glycine; glutamic acid; and threonine, wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity.

105. (New) The elastase-resistant ATIII of claim 104, wherein P3 is serine.

106. (New) The elastase-resistant ATIII of claim 104, wherein P6 is glycine.

107. (New) The elastase-resistant ATIII of claim 106, wherein P3 is serine.

108. (New) An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P3, P6, and P7 of the ATIII, wherein P3, P6, and P7 are the third, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine, wherein P6 comprises an amino acid selected from the group consisting of leucine; glycine; glutamic acid; and threonine, and wherein P7 comprises an amino acid selected from the group consisting of glutamic acid and glutamine, wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity.

B / cont.

109. (New) The elastase-resistant ATIII of claim 108, wherein P7 is glutamic acid.

110. (New) The elastase-resistant ATIII of claim 109, wherein P3 is serine, and wherein P6 is glycine.

111. (New) An elastase-resistant antithrombin III (ATIII) comprising at least five amino acid modifications, wherein the modifications occur at positions P3, P4, P5, P6, and P7 of the ATIII, wherein P3, P4, P5, P6, and P7 are the third, fourth, fifth, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is serine, wherein P4 is phenylalanine, wherein P5 is phenylalanine, wherein P6 is glycine, and wherein P7 is glutamic acid, wherein the ATIII retains an athrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity.

112. (New) An elastase-resistant antithrombin III (ATIII) comprising at least five amino acid modifications, wherein the modifications occur at positions P3, P4, P5, P6, and P7 of the ATIII, wherein P3, P4, P5, P6, and P7 are the third, fourth, fifth, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is serine, wherein P4 is alanine, wherein P5 is glutamic acid, wherein P6 is glycine, and wherein P7 is glutamic acid, wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity..

113. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P4 and P5 of the ATIII, wherein P4 and P5 are the fourth and fifth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; glycine; and proline, and wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; glycine; and proline, wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity.

114. (New). An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P4, P5, and P6 of the ATIII, wherein P4, P5, and P6 are the fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 is alanine, wherein P5 is glutamic acid; and wherein P6 is leucine, wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity.

115. (New). An elastase-resistant antithrombin III (ATIII) comprising at least four modifications, wherein the modifications occur at positions P3, P4, P5, and P6 of the ATIII, wherein P3, P4, P5, and P6 are the third, fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is isoleucine, wherein P4 is alanine, wherein P5 is glutamic acid; and wherein P6 is leucine, wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity.

116. (New) The ATIII of claim 98, wherein the ATIII is in a pharmaceutically acceptable formulation.

117. (New) The elastase-resistant ATIII of claim 98, wherein the ATIII has enhanced heparin binding activity.

118. (New) The ATIII of claim 117, wherein the ATIII is in a pharmaceutically acceptable formulation.

119. (New) The elastase-resistant ATIII of claim 98, wherein the ATIII has enhanced heparin binding activity, and wherein the ATIII has a mutation two residues subsequent to a glycosylation site.

120. (New) The ATIII of claim 119, wherein the ATIII is in a pharmaceutically acceptable formulation.

121. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two

modifications, wherein the modifications occur at positions P4 and P5 of the ATIII, wherein P4 and P5 are the fourth and fifth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; phenylalanine; glycine; and proline, and wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; phenylalanine; glycine; and proline, wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity.

B / cont.

122. (New) The elastase-resistant ATIII of claim 121, wherein the ATIII further comprises three additional modifications, wherein the modifications occur at positions P6, P7, and P8 of the ATIII, wherein P6, P7, and P8 are the sixth, seventh, and eighth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P8 is glutamic acid, wherein residue P7 comprises an amino acid selected from the group consisting of glutamic acid and glutamine, and wherein P6 comprises an amino acid selected from the group consisting of: leucine; glycine; glutamic acid; and threonine.

123. (New) The elastase-resistant ATIII of claim 121, wherein the ATIII further comprises one additional modification, wherein the modification occurs at position P3 of the ATIII, wherein P3 is the third amino acid towards the amino terminal side of the scissile bond of the reactive center , and wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine.

124. (New) An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P4, P5, and P6 of the ATIII,

wherein P4, P5, and P6 are the fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; phenylalanine; glycine; and proline, wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; phenylalanine; glycine; and proline, and wherein P6 comprises an amino acid selected from the group consisting of leucine, glycine, glutamic acid, and threonine, wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity.

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125. (New) The elastase-resistant ATIII of claim 124, wherein P6 is glycine.

126. (New) The elastase-resistant ATIII of claim 125, wherein P5 is phenylalanine or glutamic acid.

127. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P3 and P6 of the ATIII, wherein P3 and P6 are the third and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine, and wherein P6 comprises an amino acid selected from the group consisting of leucine; glycine; glutamic acid; and threonine, wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity.

128. (New) The elastase-resistant ATIII of claim 127, wherein P3 is serine.

129. (New) The elastase-resistant ATIII of claim 128, wherein P6 is glycine.

130. (New) The elastase-resistant ATIII of claim 129, wherein P3 is serine.

131. (New) An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P3, P6, and P7 of the ATIII, wherein P3, P6, and P7 are the third, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 comprises an amino acid selected from the group consisting of isoleucine; serine; glycine; and asparagine, wherein P6 comprises an amino acid selected from the group consisting of leucine; glycine; glutamic acid; and threonine, and wherein P7 comprises an amino acid selected from the group consisting of glutamic acid and glutamine, wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity.

B/cont

132. (New) The elastase-resistant ATIII of claim 131, wherein P7 is glutamic acid.

133. (New) The elastase-resistant ATIII of claim 132, wherein P3 is serine, and wherein P6 is glycine.

134. (New) An elastase-resistant antithrombin III (ATIII) comprising at least five amino acid modifications, wherein the modifications occur at positions P3, P4, P5, P6, and P7 of the ATIII, wherein P3, P4, P5, P6, and P7 are the third, fourth, fifth, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is serine, wherein P4 is phenylalanine, wherein P5 is phenylalanine,

wherein P6 is glycine, and wherein P7 is glutamic acid, wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity..

135. (New) An elastase-resistant antithrombin III (ATIII) comprising at least five amino acid modifications, wherein the modifications occur at positions P3, P4, P5, P6, and P7 of the ATIII, wherein P3, P4, P5, P6, and P7 are the third, fourth, fifth, sixth, and seventh amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is serine, wherein P4 is alanine, wherein P5 is glutamic acid, wherein P6 is glycine, and wherein P7 is glutamic acid, wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity.

B1 cont

136. (New) An elastase-resistant antithrombin III (ATIII) comprising at least two modifications, wherein the modifications occur at positions P4 and P5 of the ATIII, wherein P4 and P5 are the fourth and fifth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 comprises an amino acid selected from the group consisting of alanine; glycine; and proline, and wherein P5 comprises an amino acid selected from the group consisting of glutamic acid; glycine; and proline, wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity.

137. (New). An elastase-resistant antithrombin III (ATIII) comprising at least three modifications, wherein the modifications occur at positions P4, P5, and P6 of the ATIII,

wherein P4, P5, and P6 are the fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P4 is alanine, wherein P5 is glutamic acid; and wherein P6 is leucine, wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity.

138. (New). An elastase-resistant antithrombin III (ATIII) comprising at least four modifications, wherein the modifications occur at positions P3, P4, P5, and P6 of the ATIII, wherein P3, P4, P5, and P6 are the third, fourth, fifth, and sixth amino acids towards the amino terminal side of the scissile bond of the reactive center respectively, wherein P3 is isoleucine, wherein P4 is alanine, wherein P5 is glutamic acid; and wherein P6 is leucine, wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity.

139. (New) The ATIII of claim121, wherein the ATIII is in a pharmaceutically acceptable formulation.

140. (New) The elastase-resistant ATIII of claim 121, wherein the ATIII has enhanced heparin binding activity.

141. (New) The ATIII of claim 140, wherein the ATIII is in a pharmaceutically acceptable formulation.

142. (New) The elastase-resistant ATIII of claim 121, wherein the ATIII has enhanced heparin binding activity, and wherein the ATIII has a mutation two residues subsequent to a glycosylation site.